NEWS RELEASE

AVENZO THERAPEUTICS ADVANCES THE COMBINATION OF CDK4 SELECTIVE INHIBITOR (AVZO-023) WITH CDK2 SELECTIVE INHIBITOR (AVZO-021) IN ONGOING PHASE 1/2 ORION-1 STUDY IN HR+/HER2- BREAST CANCER

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SAN DIEGO, Calif. – April 28, 2026 – Avenzo Therapeutics, Inc. ("Avenzo"), a clinical-stage biotechnology company developing next-generation oncology therapies, today announced initiation of the combination cohort evaluating AVZO-023, its potential best-in-class cyclin-dependent kinase 4 (CDK4) selective inhibitor, in combination with AVZO-021, its potential best-in-class cyclin-dependent kinase 2 (CDK2) selective inhibitor, with fulvestrant in patients with advanced or metastatic hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2-) breast cancer in the ongoing Phase 1 portion of the ORION-1 Phase 1/2 clinical study.

"Hyperactivation of CDK2 has emerged as a key resistance mechanism to CDK4/6 inhibitors, and we believe addressing both CDK4 and CDK2 with selective inhibitors represents a rational approach to improving outcomes for patients with HR+/HER2- breast cancer," said Antonio Giordano, M.D., Ph.D., Clinical Director, Center for Cancer Therapeutic Innovation, Dana-Farber Cancer Institute. "The combination of AVZO-023 and AVZO-021 is designed to optimize CDK4 target coverage while simultaneously targeting CDK2-driven resistance, and the selective profiles of both agents may enable a tolerability advantage over less selective approaches."

The Phase 1/2 first-in-human, open-label ORION-1 clinical study is designed to assess the safety, tolerability, and preliminary clinical activity of AVZO-023 with endocrine therapy as well as the combination of AVZO-023 and AVZO-021 with endocrine therapy. The combination cohort will evaluate AVZO-023 and AVZO-021 with fulvestrant in patients with HR+/HER2- metastatic breast cancer. AVZO-021 is currently being studied in a separate Phase 1/2

clinical study in HR+/HER2- metastatic breast cancer and other advanced solid tumors, and the company plans to present updated safety and efficacy results from the Phase 1 portion of the ongoing study at the 2026 American Society of Clinical Oncology (ASCO) Annual Meeting.

“We are encouraged by the early emerging data from AVZO-023 and believe the combination of our potential best-in-class CDK4 and CDK2 selective inhibitors has the potential to meaningfully improve outcomes for patients with HR+/HER2- breast cancer,” said Mohammad Hirmand, M.D., Co-founder, and Chief Medical Officer of Avenzo Therapeutics. “We look forward to advancing this program and exploring the full potential of this novel combination.”

About Avenzo Therapeutics

Avenzo Therapeutics is a clinical-stage biotechnology company focused on developing next-generation oncology therapies for patients. The company’s pipeline includes potential best-in-class small molecules and antibody-drug conjugates (ADCs). Avenzo’s small molecule inhibitors, AVZO-021 and AVZO-023, are novel, highly potent and selective inhibitors of CDK2 and CDK4, respectively, which are key enzymes involved in cell cycle regulation. AVZO-021 is being studied in a Phase 1/2 study for the treatment of advanced solid tumors and in combinations in HR+/HER2- metastatic breast cancer. AVZO-023 is being studied in a Phase 1/2 study in combinations for the treatment of HR+/HER2- metastatic breast cancer. Avenzo’s first ADC drug candidate, AVZO-1418, is a potential best-in-class, EGFR/HER3 bispecific ADC that is being studied in a Phase 1/2 study for the treatment of advanced solid tumors. Avenzo’s second ADC drug candidate, AVZO-103, is a potential best-in-class, Nectin4/TROP2 bispecific ADC that is being studied in a Phase 1/2 study for the treatment of advanced solid tumors. Avenzo is headquartered in San Diego, California. For more information, visit us at **www.avenzotx.com** or on **LinkedIn**.

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